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EDITORIAL COMMENTARY

Post-Cooling Era: Role of Magnesium Sulphate as an Adjunct Therapy

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In 2021, 2.3 million neonates globally succumbed, with India accounting for nearly one-fifth of this burden. Of these, 20% of deaths are due to perinatal asphyxia [1].

Therapeutic hypothermia, when given to moderate to severe encephalopathic neonates after perinatal asphyxia with cord pH <7 in a tertiary care intensive unit, leads to a 42% reduction in mortality or neuro-developmental disability (RR 0.58; 95% CI 0.43–0.79) [2]. However, nearly half of the neonates who received therapeutic hypothermia died or had a severe disability at 18 to 24 mo. Hence, there is a need to continue to develop new strategies to improve outcomes in perinatal asphyxia.

In the early phase of hypoxic-ischemic encephalopathy (HIE), the overactivation of the N-methyl-D-aspartate (NMDA) receptor leads to increased calcium influx and resultant cell damage [3]. Magnesium ion gates this receptor and may protect the brain from NMDA receptor-mediated asphyxial injury and also reduces NF-kB activity, thereby downregulating the inflammatory cascade [4].

Limited data on its utility (when used alone) seems promising. A meta-analysis by Tagin et al. demonstrated a significant reduction in unfavorable composite short-term outcomes (RR 0.48, 95% CI 0.30 to 0.77) [5]. However, the evidence to date is limited in the following aspects; most studies lack numbers, have trial heterogeneity, and have limited long-term outcome data.

The study by Kumar et al. published in IJP, evaluated if adding magnesium sulfate to therapeutic hypothermia decreased the combined outcome of mortality and neurodevelopmental disability at 1 y of age [6]. This single-center study used phase-changing material for providing therapeutic hypothermia. The authors used $MgSO_4$ in a dose of 250 mg/kg initiated within 6 h of birth and two more doses 24 h apart as IV infusion over 30 min along with evaluation of serum magnesium, wherein subsequent doses were withheld if serum magnesium was >3 mg/dL.

The recent National Neonatology forum (NNF) position statement recommends servo-controlled devices for therapeutic hypothermia. If non-servo-controlled devices are used, a nurse: patient ratio of 1:1 must be ensured to maintain temperature [2]. In the present study of 134 neonates, there was no difference in the combined outcome of death or neuro-developmental disability at one-year age among the intervention (n = 14) and comparator group (n = 19) (RR 0.72; 95% CI: 0.40 to 1.30). The deaths, though fewer in the intervention group than in the comparator arm, were not statistically significant. There was no difference in abnormal neurological status at discharge. Malondialdehyde, a product of lipid peroxidation and a marker of oxidative stress, was not different in the two groups.

In the post-cooling era, neuroprotective interventions are likely adjuncts to incrementally improve outcomes beyond those achievable by hypothermia alone. Overall, the present study adds to our limited database of the role of magnesium sulfate in term neonates with perinatal asphyxia. Multicentric randomized controlled trials are needed to evaluate the benefit of magnesium therapy among these neonates in addition to therapeutic hypothermia in improving short-term or long-term outcomes.

Declarations

Conflict of Interest None.

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